

SCREEN FOR GLUTAMATE REUPTAKE INHIBITORS, STIMULATORS, AND MODULATORS

ABSTRACT OF THE DISCLOSURE

Disclosed is a method for identifying compounds that bind to or modulate a glutamate transporter. The disclosed method is useful for identifying compounds that can inhibit, stimulate, or modulate the activity of the glutamate transporter and thus affect glutamate reuptake. The method is a screening technique where compounds known to bind to glutamate receptors (for example, glutamate receptor ligands, including many agonists, and antagonists) are bound to a glutamate transporter and compounds are screened to identify those that can alter the binding of the glutamate receptor-binding compounds. Compounds shown to alter the binding of the receptor compounds from glutamate transporters in the disclosed assay can have a variety of effects on glutamate transporter activity including activation or inhibition. These compounds are expected to affect or interfere with glutamate reuptake by the glutamate transporter and thus can be used to modulate, stimulate, or inhibit glutamate reuptake. Such compounds are useful to treat various neurological diseases and conditions involving glutamate transporter and glutamate receptor activation. One of the compounds is (2*S*,4*R*)-4-methylglutamate or [³H]-(2*S*,4*R*)-4-methylglutamate. For example, excess extracellular glutamate is a cause of excessive activation of glutamate receptors. Stimulating glutamate reuptake by glutamate transporters can ameliorate excessive activation of glutamate receptors by reducing the extracellular glutamate concentration. Prodrug forms of transporter compounds are preferred for use as drugs.